C4

phenothiazine-5-dioxide, thiathrene-5-dioxide, thiathrene-5-oxide, carbazole, dibenzo[b,d]furan, dibenzo[b,d]thiophene.

REMARKS

I. Prosecution History.

The application as filed contained 19 claims. Claims 1, 5, 6, 11 have been amended herein and claims 20-31 are new. Consequently, claims 1-17 and 20-31 are pending in the instant application and are presented for reconsideration. In the Official Action (Paper No. 11) dated June 12, 2002, the examiner stated that the information disclosure statement filed on December 27, 1999 failed to comply with the provisions of 37 CFR 1.97, 1.98, and MPEP 609 because the items listed on pages 1-9 of the information disclosure statement were missing from the application.

In addition, claim 16 was rejected under 35 U.S.C. 101 as being directed to non-statutory subject matter for failing to set forth steps involved in the method or process.

Finally, the examiner rejected claims 1-19 under U.S.C. 112, second paragraph, as being indefinite for failing to point out and distinctly claim the subject matter which the applicant regards as his invention. Applicants traverse the rejections.

II. Explanation of amendments.

In this amendment, claims 18 and 19 have been canceled without prejudice as redundant. Claims 1, 5, 6, and 11 as amended find support throughout the application and are intended solely to improve the style with which the invention is claimed in accordance with the Examiners suggestions. Applicant hereby states that the amendments do not represent new matter. The Applicants do not intend by these or any other amendments to abandon the subject matter of any claim as originally presented, and reserve the right to pursue such subject matter in other applications, such as continuing applications and divisional applications. Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached pages are captioned "**Version With Markings To Show Changes Made.**" Also attached is a clean copy of the claims presently pending in the instant application.

III. The Patent Office's allegation that the information disclosure statement failed to comply with the provisions of 37 CFR 1.97, 1.98, and MPEP 609 should be withdrawn.

At page 3, paragraph 1 of the Office Action, the Patent Office alleged

> that the " information disclosure statement filed on 12/27/99 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP 609 because the items listed on pages 1-9 of the information disclosure statement are missing from the application. Correction is required."
>
> (Office action at page 3.)

Enclosed is copy of the date-stamped postcard that we received from the Patent Office indicating that the 94 references filed in the Information Disclosure Statement were received by the Patent Office. Applicants would welcome discussions with the Examiner regarding an acceptable solution to this matter.

IV. The Patent Office's rejection of claim 1 under 35 U.S.C. §101, for being directed to non-statutory subject matter should be withdrawn.

At page 3, paragraph 3 of the Office action, the Examiner also rejected claims 16 under 35 USC §101, alleging that this claim is directed to non-statutory subject matter:

> "Note that the claim is directed to methods with no method steps. As the claims do not set forth any steps involved in the method/process, it is unclear what the method/process applicant is intending to encompass. Claim 16 recites "comparing" and selecting" which do not appear to be positive method steps for a "method for identifying a non-peptidyl compound. Without setting forth any steps involved in the process;method, restuls inan improper definition of a process and is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd. App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966)."
>
> (Office action at pp. 3-4.)

The applicants respectfully traverse. The Patent Office's objection as to these steps is not at all clear. The patent literature is replete with the use of steps of "comparing" and "selecting" in a similar context to that being used in the instant application. A search of the Patent Offices's website for issued U.S. patents with process claims using both of these terms in their uncovered 21,171 issued U.S. patents. For example, U.S. Patent No. 6,449,734

recites the steps of: "comparing the sequence numbers with one another" and "selecting at least two of the sequence numbers." The Applicants respectfully submit that steps using these terms as process steps is well accepted and conventional. The citation of *Ex parte Dunki*, 153 USPQ 678 (Bd. App. 1967) and *Clinical Products, Ltd. v. Brenner*, provides little guidance to the rejection here as these cases relate the inappropriate use of "use" claim language.

V. The Patent Office's rejection under 35 U.S.C. §112, second paragraph, has been rendered moot and should be withdrawn.

At page 4, paragraph 2 of the Office action, the Patent Office rejected claims 1, 5, 6, and 11 under 35 U.S.C. § 112, second paragraph, alleging that these claims were indefinite. As the basis for rejection, the Patent Office stated that:

> Claim 1 and the dependent claims hereto are indefinite because the claim recites the term 'biological modulator' and it is unclear if applicant intends modulate to mean increase or decrease (see also claim 11). Note that only one of these terms should be recited in the claims. The claim is also indefinite as the word 'peptidyl' is misspelled as 'petidyl.'
>
> Claim 5 is indefinite for the recitation of 'so as mimic' as it appears the transitional phrase 'to' is missing.
>
> Regarding claim 6, the phrases 'for example but not limited to', 'examples include', and 'including but not limited to' renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d), see also the dependent claims hereto (see also claim 11).
>
> Claim 11 is indefinite for the recitation of 'and/or' because it is unclear if the slash mark means 'and' or 'or'. Deletion of the slash mark and recitation of just one of the terms is suggested (the dependent claims hereto are also included in this rejection).
>
> Claims 18 and 19 are indefinite because the claims do not further limit the claims from which they depend.
>
> (Office action at pp. 4-5.)

Applicants respectfully traverse the rejection. According to the Examiner the terms "biological modulator" and "compound capable of modulating the biological activity of insulin" makes it unclear if the applicant intends the term "modulate" to increase or decrease the biological activity of insulin and that only one of these terms should be recited in the claim. Applicants respectfully disagree. One of skill in the art reviewing the specification

would understand the meaning of this term as used in the claims. The term "biological modulator" is used example at page 14, line 15 and refers to compound that "may act either as agonists or antagonists" of insulin or insulin-like activity. (page 14 lines 22-23). As agonists would mimic and could potentially increase insulin or insulin-like activity and antagonists would also mimic and could potentially decrease insulin-like activity, it is clear that the term "biological modulator" may incompass both the increase or the decrease of activity and the exclusive use of either term would be inappropriate with the scope of the invention. In this context, the term conveys the nature of the invention with clarity to the reader and therefore restriction to one of these terms would be inappropriate with the scope of the invention, the claim is not indefinite, and the rejection should be withdrawn. In the event that the Examiner maintains the rejection, Applicants would welcome discussions with the Examiner regarding alternative acceptable terms that are synonymous with this term that are equally defined by the disclosure.

Claim 1 was also rejected for misspelling the term "peptidyl" as "petidyl". Claim 1 no longer recites "petidyl" but rather is now amended to recite " peptidyl" in accordance with the examiner's suggestion. The bases for rejection of this claim (and its dependent claims) for indefiniteness is moot and should be withdrawn.

Claims 5 was also rejected for improperly reciting the phrase "so as to mimic" as "so as mimic". Claim 5 no longer recites "so as mimic" but rather is now amended to recite " so as to mimic" in accordance with the examiner's suggestion. The bases for rejection of this claim for indefiniteness is moot and should be withdrawn.

Claims 6 and 11 were also rejected for including the phrases "for example but not limited to", "examples include", and "including but not limited to". Claims 6 and 11 no longer recites these phrases in accordance with the examiner's suggestion and the deleted subject matter has been added in proper dependant claims. The bases for rejection of these claims (and their dependent claims) for indefiniteness is moot and should be withdrawn.

Claim 11 was also rejected for including the term "and/or." Claim 11 no longer recites the term "and/or" but rather has been amended using Markush language to embody the same concept. The bases for rejection of these claims (and their dependent claims) for indefiniteness is moot and should be withdrawn.

Claims 18 and 19 were also rejected for not further limiting the claims from which they depend. Claims 18 and 19 are now cancelled and the bases for rejection of these claims for indefiniteness is moot and should be withdrawn.

Applicants submit that the claims are imbued with clarity and the rejection and in light of the above comments, request that the rejections based on 35 U.S.C. § 112, second paragraph should be withdrawn.

CONCLUSION

Withdrawal of the rejections and allowance all pending claims in the application are respectfully requested in view of the foregoing amendments and remarks.

An early allowance of all claims on the merits is respectfully requested. Should the examiner wish to discuss the foregoing, or any matter of form in an effort to advance this application toward allowance, the examiner is urged to telephone the undersigned at the indicated number.

Respectfully Submitted,

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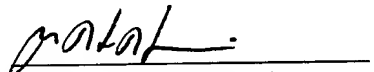
By: 
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September 12, 2002

Part/#22

Version With Markings to Show Changes Made

In the claims:

1. (Amended) A method for treating a patient suffering from one or more insulin related ailments, which method comprises the step of: administering to a patient in need thereof a therapeutically effective amount of a non-peptidyl compound that is a biological modulator of insulin activity, which compound possesses one or more ionic and hydrophobic chemical moieties spatially located so as to mimic the spatial location of at least an ionic or a hydrophobic amino acid residue of insulin, which amino acids are associated with the binding of insulin to its receptor.

5. (Amended) A method according to claim 1, wherein the non-peptidyl compound possesses ionic and hydrophobic chemical moieties spatially located so as to mimic ionic and hydrophobic residues associated with at least one of the following groups of amino acid residues:

(i.) A21 Asn, B21 Glu, A17 Glu, B24 Phe, B25 Phe;

(ii.) A21 Asn, B21 Glu, B24 Phe, B25 Phe;

(iii.) A21 Asn, B21 Glu, B24 Phe, B25 Phe, A1 Gly, A2 Ile, A3 Val;

(iv.) A21 Asn, B21 Glu, A17 Glu, A19 Tyr, A1 Gly, A2 Ile, A3 Val;

(v.) A21 Asn, B21 Glu, A17 Glu, B12 Val, A1 Gly, A2 Ile, A3 Val;

(vi.) A21 Asn, B21 Glu, B12 Val, A1 Gly, A2 Ile, A3 Val;

(vii.) A21 Asn, B21 Glu, A17 Glu, B16 Tyr, A1 Gly, A2 Ile, A3 Val;

(viii) A21 Asn, B21 Glu, A17 Glu, A19 Tyr, B12 Val, B16 Tyr;

(ix.) A21 Asn, B21 Glu, A19 Tyr, B12 Val, B16 Tyr;

(x.) A21 Asn, B21 Glu, A17 Glu, B24 Phe, B25 Phe, A19 Tyr, B12 Val, B16 Tyr;

(xi.) A21 Asn, B21 Glu, B24 Phe, B25 Phe, A19 Tyr, B12 Val, B16 Tyr;

(xii) A21 Asn, B21 Glu, B24 Phe, B25 Phe, B12 Val, B16 Tyr;

(xiii.) A21 Asn, B21 Glu, A17 Glu, B24 Phe, B25 Phe, A19 Tyr;

(xiv.) A21 Asn, B21 Glu, B24 Phe, B25 Phe, A19 Tyr;

(xv.) A21 Asn, A17 Glu, B24 Phe, B25 Phe, A19 Tyr;

(xvi.) B21 Glu, A17 Glu, B24 Phe, B25 Phe, A19 Tyr;

(xvii.) A21 Asn, B21 Glu, A17 Glu, B24 Phe, B25 Phe, B12 Val;

(xviii.) A21 Asn, B21 Glu, B24 Phe, B25 Phe, B12 Val;

(xix.) A21 Asn, A17 Glu, B24 Phe, B25 Phe, B12 Val;

(xx.) B21 Glu, A17 Glu, B24 Phe, B25 Phe, B12 Val;

(xxi.) A21 Asn, B21 Glu, A17 Glu, B24 Phe, B25 Phe, B16 Tyr;

(xxii.) A21 Asn, B21 Glu, B24 Phe, B25 Phe, B16 Tyr;

(xxiii.) A21 Asn, A17 Glu, B24 Phe, B25 Phe, B16 Tyr;

(xxiv.) B21 Glu, A17 Glu, B24 Phe, B25 Phe, B16 Tyr;

(xxv.) A21 Asn, B21 Glu, A17 Glu, B24 Phe, A19 Tyr, B12 Val, B16 Tyr;

(xxvi.) A21 Asn, B21 Glu, B24 Phe, A19 Tyr, B12 Val, B16 Tyr;

(xxvii.)A21 Asn, A17 Glu, B24 Phe, A19 Tyr, B12 Val, B16 Tyr;

(xxviii.) B21 Glu, A17 Glu, B24 Phe, A19 Tyr, B12 Val, B16 Tyr;

(xxix.) A21 Asn, B21 Glu, A17 Glu, B25 Phe, A19 Tyr, B12 Val, B16 Tyr;

(xxx.) A21 Asn, B21 Glu, B25 Phe, A19 Tyr, B12 Val, B16 Tyr;

(xxxi.) A21 Asn, A17 Glu, B25 Phe, A19 Tyr, B12 Val, B16 Tyr; or

(xxxii.)B21 Glu, A17 Glu, B25 Phe, A19 Tyr, B12 Val.

6. (Amended) A method according to claim 1, wherein the non-peptidyl compound has the following formula:

$AXYXZ_n$ (formula 1)

where A is W or VXW;

V is V_1 or V_2;

V is substituted with up to two X groups;

V_1 is a phenyl or 6 membered heteroaromatic ring, optionally substituted with up to 5 R_1 groups, [for example but not being limited to benzene, pyridine, pyridazine, pyrimidine, pyrazine, triazine];

V_2 is a 5 member ring system which may incorporate up to 4 hetero atoms which may be independently a nitrogen atom, a nitrogen atom optionally substituted with R_2, oxygen or sulfur, [for example but not being limited to cyclopenta 1,3 diene, pyrrole, furan, thiophene, exazole, isoxazole, pyrazole, imidazole, thiazole, isothiazole or triazole], the ring system being optionally substituted with up to 4 R_1 groups;

W is W_1 or W_2 or W_3;

W is substituted with up to two X groups;

W_1 is V_1;

W_2 is a fused bicyclic ring system comprising rings of 5 or 6 atoms, which may incorporate up to 4 hetero atoms, which may be independently a nitrogen atom, a nitrogen atom optionally substituted with R_2, oxygen or sulfur, the system being optionally substituted with up to seven R_1 groups [and examples include, but are not being limited to naphthalene, quinoline, isoquinoline, phthalazine, naphthyridine, quinoxaline, quinazoline, cinnoline, pteridine, indole, benzothiophene, benzofuran, benzimidazole, indazole, benzoxazole, benzisooxazole, benzthiazole, benzisothiazole, purine, indoline, isoindoline];

W_3 is $-N(R_2)R'_2$;

R_1 is independently H, OH, alkyl, alkenyl, alkynyl, alkoxy, alkanol, hydroxyalkoxy, haloalkyl, haloalkoxy, halogen, SH, thioalkyl, cyano (-CN), $N(R_2)R'_2$, phenyl, phenyl optionally substituted with up to five alkyl groups of 1 to 3 carbon atoms or up to five halogen atoms, benzyl, phenethyl, nitro, $-COR_3$, $-R_5COR_3$, $-R_5SOR_3$, $-R_5SO_2R_3$, $-SO_2N(R_2)R'_2$ or azido;

R_2 and R'_2 are independently H, alkyl of 1 to 6 carbon atoms, alkenyl of 3 to 6 carbon atoms, alkynyl of 3 to 6 carbons, hydroxyalkyl of 2 to 6 carbons, alkoxy of 2 to 6 carbons, haloalkyl, haloalkenyl, haloalkoxy, benzyl, benzyl optionally substituted with up to four R_1 groups, phenylethyl, phenylethyl optionally substituted with up to four R_1 groups, arylalkyl, and where R_2 and R'_2 can also be joined to form cyclic structures [including, but not limited to pyrrolidine, piperidine, hexahydro1H azepine, morpholine or piperazine];

R_3 is independently H, OH, alkyl, alkenyl, alkynyl, alkoxy, alkanol, hydroxyalkoxy, $-R_4N(R_2)R'_2$, mesyl, triflouromesyl, $-NHSO_2CH_3$ or $-NHSO_2CF_3$;

R_4 is independently a bond, alkyl, alkenyl or alkynyl;

X is independently, a bond, $-R_4N(R_2)R_4-$, $-R_4N=NR_4-$, $-R_4N(R_2)-N(R_2)R_4-$, $-R_4OR_4-$, $-R_4SR_4-$, $-R_5-$, $-R_5O-$, $-R_5S-$, $-R_5N(R_2)-$, -SO-, sulfonyl ($-SO_2-$), -CO-, -CONH-, -NHCONH-, -NHCO-, -CONHCO-, $-CON(R_2)-$, $-R_5COR_5-$, $-R_5COR_5N(R_2)R_5-$, $-N(R_2)CO-$ or $-R_4N(R_2)R_4COR_4-$;

R_5 is independently alkyl, alkenyl, alkynyl, alkoxy, alkanol, hydroxyalkoxy;

Y is either Y_1, Y_2 or Y_3;

Y is substituted with at least two, but optionally up to four X linking groups;

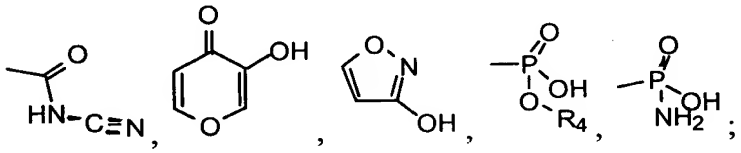
Y_1 is a fused bicyclic ring system comprising rings of 5 or 6 atoms which may incorporate up to 4 hetero atoms, which may be independently a nitrogen atom, a nitrogen atom optionally substituted with R_2, oxygen or sulfur, the ring system optionally independently incorporating a sulfoxide (SO), sulfone (SO_2) or carbonyl (CO) group and optionally up to seven R_1 groups[, for example but not limited to croman, isochroman, benzofuran, cromene, 1,2,3,4-tetrahydronaphthalene, 1,4-dihydronaphthalene, indan, indene, benzopiperidine, indoline, isoindoline, quinoline, isoquinoline, phthalazine, naphthyridine, quinoxaline, quinazoline, cinnoline or pteridine, coumarin or 2,3-dihydrocoumarin];

Y_2 is a 6:6:6 or a 6:5:6 fused tricyclic system which may incorporate up to 4 hetero atoms which may be independently a nitrogen atom, a nitrogen atom optionally substituted with R_2, oxygen or sulfur, the ring system optionally independently incorporating a sulfoxide (SO), sulfone (SO_2) or carbonyl (CO) group, and the ring system being substituted with at least two, but optionally up to four X linking groups and optionally up to seven R_1 groups [and thus examples include, but are not limited to 9H-xanthene, 9H-xanthene, phenoxathiin, phenoxathiin-10-oxide, phenoxathiin-10-dioxide, acridine, phenazine, phenothiazine, phenoxazine, phenothiazine 5-oxide, phenothiazine-5-dioxide, thiathrene-5-dioxide, thiathrene-5-oxide, carbazole, dibenzo[b,d]furan, dibenzo[b,d]thiophene];

Y_3 is V_1;

Z is independently $-R_6COOH$, $-R_6SO_3H$, $-R_6NO_2$, $-R_6SO_2H$, $-R_6SO_2NHR_2$; $-R_7SO_2NHCOR_4$ -N-trifluoromesylsulfonamidate, -OH, -2-yl-hydroxyethanoic acid (-CH(OH)COOH), -3-yl-2-hydroxypropanoic acid ($-CH_2CH(OH)COOH$) -2-yl-2-

hydroxypropanoic acid (-$CH(CH_3)(OH)COOH$), -3-yl-2,3-dihydroxypropanoic acid (-$CH(OH)CH(OH)COOH$), -2-yl-2,3-dihydroxypropanoic acid (-$C(CH_2(OH))(OH)COOH$), -3-yl-2-hydroxypropan-3-one-1-oic acid (-$COCH(OH)COOH$, 2-yl-2-hydroxypropandioic acid (-$C(COOH)(OH)COOH$), -2-yl-propandioic acid (-$C(COOH)(H)COOH$), -4-yl-2-hydroxybutan-4-one-1-oic acid (-$COCH_2CH(OH)COOH$, 2-yl-2-hydroxybutan-1,4-dioic acid (-$C(OH)(COOH)CH_2COOH$), 3-yl-2-hydroxybutan-1,4-dioic acid (-$CH(CH(OH)COOH)COOH$), 5-yl-tetrazole,



R_6 is independently a bond, alkyl, alkenyl, alkynyl, alkoxy, -$CO(CH_2)_n$-, where n is an integer between 0 and 4, alkanoic, alkenoic or alkynoic;

with the exception that where W_1 is an optionally substituted phenyl then Y_1 cannot be an optionally substituted phenyl.

11. (Amended) A pharmaceutical composition comprising at least a chemical compound capable of modulating the biological activity of insulin, and a second composition selected from the group consisting of a pharmaceutically acceptable carrier, a [and/or] diluent, and combinations thereof; wherein said compound has the following general formula.

$AXYXZ_n$ (formula 1)

where A is W or VXW;

V is V_1 or V_2;

V is substituted with up to two X groups;

V_1 is a phenyl or 6 membered heteroaromatic ring, optionally substituted with up to 5 R_1 groups[, for example but not being limited to benzene, pyridine, pyridazine, pyrimidine, pyrazine, triazine];

V_2 is a 5 member ring system which may incorporate up to 4 hetero atoms which may be independently a nitrogen atom, a nitrogen atom optionally substituted with R_2, oxygen or sulfur, [for example but not being limited to cyclopenta-1,3-diene, pyrrole, furan, thiophene, exazole, isoxazole, pyrazole, imidazole, thiazole,

isothiazole or triazole,] the ring system being optionally substituted with up to 4 R_1 groups;

W is W_1 or W_2 or W_3;

W is substituted with up to two X groups;

W_1 is V_1;

W_2 is a fused bicyclic ring system comprising rings of 5 or 6 atoms, which may incorporate up to 4 hetero atoms, which may be independently a nitrogen atom, a nitrogen atom optionally substituted with R_2, oxygen or sulfur, the system being optionally substituted with up to seven R_1 groups [and examples include, but are not limited to naphthalene, quinoline, isoquinoline, phthalazine, naphthyridine, quinoxaline, quinazoline, cinnoline, pteridine, indole, benzothiophene, benzofuran, benzimidazole, indazole, benzoxazole, benzisooxazole, benzthiazole, benzisothiazole, purine, indoline, isoindoline];

W_3 is $-N(R_2)R'_2$;

R_1 is independently H, OH, alkyl, alkenyl, alkynyl, alkoxy, alkanol, hydroxyalkoxy, haloalkyl, haloalkoxy, halogen, SH, thioalkyl, cyano (-CN), $N(R_2)R'_2$, phenyl, phenyl optionally substituted with up to five alkyl groups of 1 to 3 carbon atoms or up to five halogen atoms, benzyl, phenethyl, nitro, $-COR_3$, $-R_5COR_3$, $-R_5SOR_3$, $-R_5SO_2R_3$, $-SO_2N(R_2)R'_2$ or azido;

R_2 and R'_2 are independently H, alkyl of 1 to 6 carbon atoms, alkenyl of 3 to 6 carbon atoms, alkynyl of 3 to 6 carbons, hydroxyalkyl of 2 to 6 carbons, alkoxy of 2 to 6 carbons, haloalkyl, haloalkenyl, haloalkoxy, benzyl, benzyl optionally substituted with up to four R_1 groups, phenylethyl, phenylethyl optionally substituted with up to four R_1 groups, arylalkyl, and where R_2 and R'_2 can also be joined to form cyclic structures [including but not limited to pyrrolidine, piperidine, hexahydro1H-azepine, morpholine or piperazine];

R_3 is independently H, OH, alkyl, alkenyl, alkynyl, alkoxy, alkanol, hydroxyalkoxy, $-R_4N(R_2)R'_2$, mesyl, triflouromesyl, $-NHSO_2CH_3$ or $-NHSO_2CF_3$;

R_4 is independently a bond, alkyl, alkenyl or alkynyl;

X is independently, a bond, $-R_4N(R_2)R_4-$, $-R_4N{=}NR_4-$, $-R_4N(R_2)-N(R_2)R_4-$, $-R_4OR_4-$, $-R_4SR_4-$, $-R_5-$, $-R_5O-$, $-R_5S-$, $-R_5N(R_2)-$, -SO-, sulfonyl ($-SO_2-$), -CO-, -CONH-, -

NHCONH-, -NHCO-, -CONHCO-, -CON(R_2)-, -R_5COR_5-, -$R_5COR_5N(R_2)R_5$-, -$N(R_2)CO$- or -$R_4N(R_2)R_4COR_4$-;

R_5 is independently alkyl, alkenyl, alkynyl, alkoxy, alkanol, hydroxyalkoxy;

Y is either Y_1, Y_2 or Y_3;

Y is substituted with at least two, but optionally up to four X linking groups;

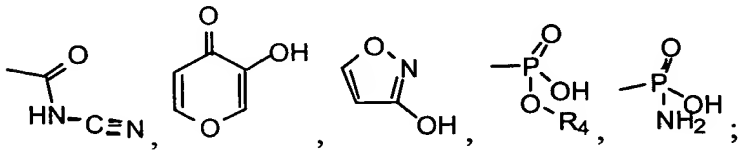
Y_1 is a fused bicyclic ring system comprising rings of 5 or 6 atoms which may incorporate up to 4 hetero atoms, which may be independently a nitrogen atom, a nitrogen atom optionally substituted with R_2, oxygen or sulfur, the ring system optionally independently incorporating a sulfoxide (SO), sulfone (SO_2) or carbonyl (CO) group and optionally up to seven R_1 groups[, for example but not limited to croman, isochroman, benzofuran, cromene, 1,2,3,4-tetrahydronaphthalene, 1,4-dihydronaphthalene, indan, indene, benzopiperidine, indoline, isoindoline, quinoline, isoquinoline, phthalazine, naphthyridine, quinoxaline, quinazoline, cinnoline or pteridine, coumarin or 2,3-dihydrocoumarin];

Y_2 is a 6:6:6 or a 6:5:6 fused tricyclic system which may incorporate up to 4 hetero atoms which may be independently a nitrogen atom, a nitrogen atom optionally substituted with R_2, oxygen or sulfur, the ring system optionally independently incorporating a sulfoxide (SO), sulfone (SO_2) or carbonyl (CO) group, and the ring system being substituted with at least two, but optionally up to four X linking groups and optionally up to seven R_1 groups [and thus examples include, but are not limited to 9H-xanthone, 9H-xanthene, phenoxathaiin, phenoxathiin-10-oxide, phenoxathiin-10-dioxide, acridine, phenazine, phenothiazine, phenoxazine, phenothiazine-5-oxide, phenothiazine-5-dioxide, thiathrene-5-dioxide, thiathrene-5-oxide, carbazole, dibenzo[b,d]furan, dibenzo[b,d]thiophene];

Y_3 is V_1;

Z is independently -R_6COOH, -R_6SO_3H, -R_6NO_2, -R_6SO_2H, -$R_6SO_2NHR_2$; -$R_7SO_2NHCOR_4$ -N-trifluoromesylsulfonamidate, -OH, -2-yl-hydroxyethanoic acid (-CH(OH)COOH), -3-yl-2-hydroxypropanoic acid (-CH_2CH(OH)COOH) -2-yl-2-hydroxypropanoic acid (-$CH(CH_3)$(OH)COOH), -3-yl-2,3-dihydroxypropanoic acid (-CH(OH)CH(OH)COOH), -2-yl-2,3-dihydroxypropanoic acid (-$C(CH_2(OH))$(OH)COOH), -3-yl-2-hydroxypropan-3-one-1-oic acid (-COCH(OH)COOH, 2-yl-2-hydroxypropandioic acid (-C(COOH)(OH)COOH), -2-

yl-propandioic acid (-C(COOH)(H)COOH), -4-yl-2-hydroxybutan-4-one-1-oic acid (-$COCH_2CH(OH)COOH$, 2-yl-2-hydroxybutan-1,4-dioic acid (-$C(OH)(COOH)CH_2COOH$), 3-yl-2-hydroxybutan-1,4-dioic acid (-$CH(CH(OH)COOH)COOH$), 5-yl-tetrazole,



R_6 is independently a bond, alkyl, alkenyl, alkynyl, alkoxy, $-CO(CH_2)_n-$, where n is an integer between 0 and 4, alkanoic, alkenoic or alkynoic;

with the exception that where W_1 is an optionally substituted phenyl then Y_1 cannot be an optionally substituted phenyl.

18. (Cancelled)

19. (Cancelled)

20. (New) A method according to claim 6 wherein V_1 is selected from the group: benzene, pyridine, pyridazine, pyrimidine, pyrazine, triazine.

21. (New) A method according to claim 6 wherein V_2 is selected from the group: cyclopenta-1,3-diene, pyrrole, furan, thiophene, oxazole, isoxazole, pyrazole, imidazole, thiazole, isothiazole or triazole, optionally substituted with up to 4 R_1 groups.

22. (New) A method according to claim 6 wherein W_2 is selected, from the group: naphthalene, quinoline, isoquinoline, phthalazine, naphthyridine, quinoxaline, quinazoline, cinnoline, pteridine, indole, benzothiophene, benzofuran, benzimidazole, indazole, benzoxazole, benzisooxazole, benzthiazole, benzisothiazole, purine, indoline, isoindoline.

23. (New) A method according to claim 6 wherein R_2 and R'_2 are joined to form cyclic structures selected from the group: pyrrolidine, piperidine, hexahydro-1H-azepine, morpholine or piperazine.

24. (New) A method according to claim 6 wherein Y_1 is selected from the group: croman, isochroman, benzofuran, cromene, 1,2,3,4-tetrahydronaphthalene, 1,4-dihydronaphthalene, indan, indene, benzopiperidine, indoline, isoindoline, quinoline,

isoquinoline, phthalazine, naphthyridine, quinoxaline, quinazoline, cinnoline or pteridine, coumarin or 2,3-dihydrocoumarin.

25. (New) A method according to claim 6 wherein Y_2 is selected from the group: 9H-xanthone, 9H-xanthene, phenoxathiin, phenoxathiin-10-oxide, phenoxathiin-10-dioxide, acridine, phenazine, phenothiazine, phenoxazine, phenothiazine-5-oxide, phenothiazine-5-dioxide, thiathrene-5-dioxide, thiathrene-5-oxide, carbazole, dibenzo[b,d]furan, dibenzo[b,d]thiophene.

26. (New) A pharmaceutical composition according to claim 11 wherein V_1 is selected from the group: benzene, pyridine, pyridazine, pyrimidine, pyrazine, triazine.

27. (New) A pharmaceutical composition according to claim 11 wherein V_2 is selected from the group: cyclopenta-1,3-diene, pyrrole, furan, thiophene, oxazole, isoxazole, pyrazole, imidazole, thiazole, isothiazole or triazole, optionally substituted with up to 4 R_1 groups.

28. (New) A pharmaceutical composition according to claim 11 wherein W_2 is selected, from the group: naphthalene, quinoline, isoquinoline, phthalazine, naphthyridine, quinoxaline, quinazoline, cinnoline, pteridine, indole, benzothiophene, benzofuran, benzimidazole, indazole, benzoxazole, benzisooxazole, benzthiazole, benzisothiazole, purine, indoline, isoindoline.

29. (New) A pharmaceutical composition according to claim 11 wherein R_2 and R'_2 are joined to form cyclic structures selected from the group: pyrrolidine, piperidine, hexahydro-1H-azepine, morpholine or piperazine.

30. (New) A pharmaceutical composition according to claim 11 wherein Y_1 is selected from the group: croman, isochroman, benzofuran, cromene, 1,2,3,4-tetrahydronaphthalene, 1,4-dihydronaphthalene, indan, indene, benzopiperidine, indoline, isoindoline, quinoline, isoquinoline, phthalazine, naphthyridine, quinoxaline, quinazoline, cinnoline or pteridine, coumarin or 2,3-dihydrocoumarin.

31. (New) A pharmaceutical composition according to claim 11 wherein Y_2 is selected from the group: 9H-xanthone, 9H-xanthene, phenoxathiin, phenoxathiin-10-oxide, phenoxathiin-10-dioxide, acridine, phenazine, phenothiazine, phenoxazine, phenothiazine-5-

oxide, phenothiazine-5-dioxide, thiathrene-5-dioxide, thiathrene-5-oxide, carbazole, dibenzo[b,d]furan, dibenzo[b,d]thiophene.

APPENDIX OF CLAIMS PENDING

1. A method for treating a patient suffering from one or more insulin related ailments, which method comprises the step of: administering to a patient in need thereof a therapeutically effective amount of a non-peptidyl compound that is a biological modulator of insulin activity, which compound possesses one or more ionic and hydrophobic chemical moieties spatially located so as to mimic the spatial location of at least an ionic or a hydrophobic amino acid residue of insulin, which amino acids are associated with the binding of insulin to its receptor.

2. A method according to claim 1, wherein the ionic amino acid residue is selected from the group comprising: A21 Asn, B21 Glu and A17 Glu.

3. A method according to claim 1, wherein the ionic and hydrophobic amino acid residue(s) is(are) selected from the group consisting of: A21 Asn, B21 Glu, A17 Glu, B24 Phe, B25 Phe, A19 Tyr, B12 Val, B16 Tyr, A2 Ile, A3 Val and A1 Gly.

4. A method according to claim 1, wherein at least one amino acid is selected from the group comprising: A17 Glu, B21 Glu and A21 Asn; and at least one amino acid is selected from the group comprising: B24 Phe, B25 Phe, A19 Tyr, B12 Val and B12 Tyr.

5. A method according to claim 1, wherein the non-peptidyl compound possesses ionic and hydrophobic chemical moieties spatially located so as to mimic ionic and hydrophobic residues associated with at least one of the following groups of amino acid residues:

(i.) A21 Asn, B21 Glu, A17 Glu, B24 Phe, B25 Phe;

(ii.) A21 Asn, B21 Glu, B24 Phe, B25 Phe;

(iii.) A21 Asn, B21 Glu, B24 Phe, B25 Phe, A1 Gly, A2 Ile, A3 Val;

(iv.) A21 Asn, B21 Glu, A17 Glu, A19 Tyr, A1 Gly, A2 Ile, A3 Val;

(v.) A21 Asn, B21 Glu, A17 Glu, B12 Val, A1 Gly, A2 Ile, A3 Val;

(vi.) A21 Asn, B21 Glu, B12 Val, A1 Gly, A2 Ile, A3 Val;

(vii.) A21 Asn, B21 Glu, A17 Glu, B16 Tyr, A1 Gly, A2 Ile, A3 Val;

(viii) A21 Asn, B21 Glu, A17 Glu, A19 Tyr, B12 Val, B16 Tyr;

(ix.) A21 Asn, B21 Glu, A19 Tyr, B12 Val, B16 Tyr;

(x.) A21 Asn, B21 Glu, A17 Glu, B24 Phe, B25 Phe, A19 Tyr, B12 Val, B16 Tyr;

(xi.) A21 Asn, B21 Glu, B24 Phe, B25 Phe, A19 Tyr, B12 Val, B16 Tyr;

(xii) A21 Asn, B21 Glu, B24 Phe, B25 Phe, B12 Val, B16 Tyr;

(xiii.) A21 Asn, B21 Glu, A17 Glu, B24 Phe, B25 Phe, A19 Tyr;

(xiv.) A21 Asn, B21 Glu, B24 Phe, B25 Phe, A19 Tyr;

(xv.) A21 Asn, A17 Glu, B24 Phe, B25 Phe, A19 Tyr;

(xvi.) B21 Glu, A17 Glu, B24 Phe, B25 Phe, A19 Tyr;

(xvii.) A21 Asn, B21 Glu, A17 Glu, B24 Phe, B25 Phe, B12 Val;

(xviii.) A21 Asn, B21 Glu, B24 Phe, B25 Phe, B12 Val;

(xix.) A21 Asn, A17 Glu, B24 Phe, B25 Phe, B12 Val;

(xx.) B21 Glu, A17 Glu, B24 Phe, B25 Phe, B12 Val;

(xxi.) A21 Asn, B21 Glu, A17 Glu, B24 Phe, B25 Phe, B16 Tyr;

(xxii.) A21 Asn, B21 Glu, B24 Phe, B25 Phe, B16 Tyr;

(xxiii.) A21 Asn, A17 Glu, B24 Phe, B25 Phe, B16 Tyr;

(xxiv.) B21 Glu, A17 Glu, B24 Phe, B25 Phe, B16 Tyr;

(xxv.) A21 Asn, B21 Glu, A17 Glu, B24 Phe, A19 Tyr, B12 Val, B16 Tyr;

(xxvi.) A21 Asn, B21 Glu, B24 Phe, A19 Tyr, B12 Val, B16 Tyr;

(xxvii.)A21 Asn, A17 Glu, B24 Phe, A19 Tyr, B12 Val, B16 Tyr;

(xxviii.) B21 Glu, A17 Glu, B24 Phe, A19 Tyr, B12 Val, B16 Tyr;

(xxix.) A21 Asn, B21 Glu, A17 Glu, B25 Phe, A19 Tyr, B12 Val, B16 Tyr;

(xxx.) A21 Asn, B21 Glu, B25 Phe, A19 Tyr, B12 Val, B16 Tyr;

(xxxi.) A21 Asn, A17 Glu, B25 Phe, A19 Tyr, B12 Val, B16 Tyr; or

(xxxii.)B21 Glu, A17 Glu, B25 Phe, A19 Tyr, B12 Val.

6. A method according to claim 1, wherein the non-peptidyl compound has the following formula:

$AXYXZ_n$ (formula 1)

where A is W or VXW;

V is V_1 or V_2;

V is substituted with up to two X groups;

V_1 is a phenyl or 6 membered heteroaromatic ring, optionally substituted with up to 5 R_1 groups;

V_2 is a 5 member ring system which may incorporate up to 4 hetero atoms which may be independently a nitrogen atom, a nitrogen atom optionally substituted with R_2, oxygen or sulfur, the ring system being optionally substituted with up to 4 R_1 groups;

W is W_1 or W_2 or W_3;

W is substituted with up to two X groups;

W_1 is V_1;

W_2 is a fused bicyclic ring system comprising rings of 5 or 6 atoms, which may incorporate up to 4 hetero atoms, which may be independently a nitrogen atom, a nitrogen atom optionally substituted with R_2, oxygen or sulfur, the system being optionally substituted with up to seven R_1 groups;

W_3 is $-N(R_2)R'_2$;

R_1 is independently H, OH, alkyl, alkenyl, alkynyl, alkoxy, alkanol, hydroxyalkoxy, haloalkyl, haloalkoxy, halogen, SH, thioalkyl, cyano (-CN), $N(R_2)R'_2$, phenyl, phenyl optionally substituted with up to five alkyl groups of 1 to 3 carbon atoms or up to five halogen atoms, benzyl, phenethyl, nitro, $-COR_3$, $-R_5COR_3$, $-R_5SOR_3$, $-R_5SO_2R_3$, $-SO_2N(R_2)R'_2$ or azido;

R_2 and R'_2 are independently H, alkyl of 1 to 6 carbon atoms, alkenyl of 3 to 6 carbon atoms, alkynyl of 3 to 6 carbons, hydroxyalkyl of 2 to 6 carbons, alkoxy of 2 to 6 carbons, haloalkyl, haloalkenyl, haloalkoxy, benzyl, benzyl optionally substituted with up to four R_1 groups, phenylethyl, phenylethyl optionally substituted with up to four R_1 groups, arylalkyl, and where R_2 and R'_2 can also be joined to form cyclic structures;

R_3 is independently H, OH, alkyl, alkenyl, alkynyl, alkoxy, alkanol, hydroxyalkoxy, $-R_4N(R_2)R'_2$, mesyl, triflouromesyl, $-NHSO_2CH_3$ or $-NHSO_2CF_3$;

R_4 is independently a bond, alkyl, alkenyl or alkynyl;

X is independently, a bond, $-R_4N(R_2)R_4-$, $-R_4N=NR_4-$, $-R_4N(R_2)-N(R_2)R_4-$, $-R_4OR_4-$, $-R_4SR_4-$, $-R_5-$, $-R_5O-$, $-R_5S-$, $-R_5N(R_2)-$, -SO-, sulfonyl ($-SO_2-$), -CO-, -CONH-, -NHCONH-, -NHCO-, -CONHCO-, $-CON(R_2)-$, $-R_5COR_5-$, $-R_5COR_5N(R_2)R_5-$, $-N(R_2)CO-$ or $-R_4N(R_2)R_4COR_4-$;

R_5 is independently alkyl, alkenyl, alkynyl, alkoxy, alkanol, hydroxyalkoxy;

Y is either Y_1, Y_2 or Y_3;

Y is substituted with at least two, but optionally up to four X linking groups;

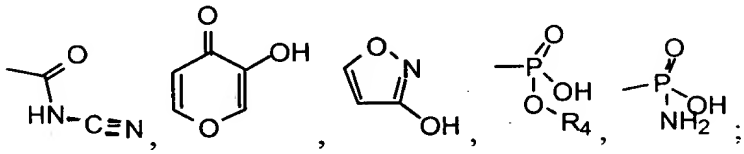
Y_1 is a fused bicyclic ring system comprising rings of 5 or 6 atoms which may incorporate up to 4 hetero atoms, which may be independently a nitrogen atom, a nitrogen atom optionally substituted with R_2, oxygen or sulfur, the ring system optionally independently incorporating a sulfoxide (SO), sulfone (SO_2) or carbonyl (CO) group and optionally up to seven R_1 groups;

Y_2 is a 6:6:6 or a 6:5:6 fused tricyclic system which may incorporate up to 4 hetero atoms which may be independently a nitrogen atom, a nitrogen atom optionally substituted with R_2, oxygen or sulfur, the ring system optionally independently incorporating a sulfoxide (SO), sulfone (SO_2) or carbonyl (CO) group, and the ring system being substituted with at least two, but optionally up to four X linking groups and optionally up to seven R_1 groups;

Y_3 is V_1;

Z is independently $-R_6COOH$, $-R_6SO_3H$, $-R_6NO_2$, $-R_6SO_2H$, $-R_6SO_2NHR_2$; $-R_7SO_2NHCOR_4$ -N-trifluoromesylsulfonamidate, -OH, -2-yl-hydroxyethanoic acid (-CH(OH)COOH), -3-yl-2-hydroxypropanoic acid ($-CH_2CH(OH)COOH$) -2-yl-2-hydroxypropanoic acid ($-CH(CH_3)(OH)COOH$), -3-yl-2,3-dihydroxypropanoic acid (-CH(OH)CH(OH)COOH), -2-yl-2,3-dihydroxypropanoic acid ($-C(CH_2(OH))(OH)COOH$), -3-yl-2-hydroxypropan-3-one-1-oic acid (-COCH(OH)COOH, 2-yl-2-hydroxypropandioic acid (-C(COOH)(OH)COOH), -2-yl-propandioic acid (-C(COOH)(H)COOH), -4-yl-2-hydroxybutan-4-one-1-oic acid ($-COCH_2CH(OH)COOH$, 2-yl-2-hydroxybutan-1,4-dioic acid (-

C(OH)(COOH)CH_2COOH), 3-yl-2-hydroxybutan-1,4-dioic acid (-CH(CH(OH)COOH)COOH), 5-yl-tetrazole,



R_6 is independently a bond, alkyl, alkenyl, alkynyl, alkoxy, $-CO(CH_2)_n-$, where n is an integer between 0 and 4, alkanoic, alkenoic or alkynoic;

with the exception that where W_1 is an optionally substituted phenyl then Y_1 cannot be an optionally substituted phenyl.

7. A method according to claim 6, wherein the non-peptidyl compound is a dimer or heterodimer wherein the compounds are joined through a X linking group by way of their V or W groups.

8. A method according to claim 6, wherein when V is V_1 or V_2, then:

V_1 is selected from the group consisting of, benzene, pyridine, pyridazine, pyrimidine, pyrazine or triazine and is optionally substituted with up to 5 R_1 groups; and

V_2 is selected from the group consisting of, cyclopenta-1,3-diene, pyrrole, furan, thiophene, oxazole, isoxazole, pyrazole, imidazole, thiazole, isothiazole or triazole and is optionally substituted with up to 4 R_1 groups;

and W is W_2 then

W_2 is selected from the group consisting of naphthalene, quinoline, isoquinoline, phthalazine, naphthyridine, quinoxaline, quinazoline, cinnoline, pteridine, indole, benzothiophene, benzofuran, benzimidazole, indazole, benzoxazole, benzisooxazole, benzthiazole, benzisothiazole, purine, indoline or isoindoline and is optionally substituted with up to seven R_1 groups;

and Y is either Y_1 or Y_2 then

Y_1 is selected from the group consisting of croman, isochroman, benzofuran, cromene, 1,2,3,4-tetrahydronaphthalene, 1,4-dihydronaphthalene, indan, indene, benzopiperidine, indoline, isoindoline, quinoline, isoquinoline, phthalazine, naphthyridine, quinoxaline, quinazoline, cinnoline or pteridine, coumarin or 2,3-dihydrocoumarin and is optionally substituted with up to seven R_1 groups; and

Y_2 is selected from the group consisting of 9H-xanthone, 9H-xanthene, phenoxathiin, phenoxathiin-10-oxide, phenoxathiin-10-dioxide, acridine, phenazine, phenothiazine, phenoxazine, phenothiazine-5-oxide, phenothiazine-5-dioxide, thiathrene-5-dioxide, thiathrene-5-oxide, carbazole, dibenzo[b,d]furan or dibenzo[b,d]thiophene and is optionally substituted with up to seven R_1 groups.

9. A method according to claim 6, wherein when A is VXW then:

V is phenyl or pyrazole, optionally substituted with up to 5 R_1 groups;

and when A is W or VXW then W is W_1, W_2 or W_3 wherein

W_1 is phenyl optionally substituted with up to 5 R_1 groups;

W_2 is naphthalene or quinoline optionally substituted with up to seven R_1 groups wherein R_1 is independently H, OH, methyl, ethyl, propyl, nitro, methoxy, ethoxy, 2-hydroxyethoxy, chloro, fluoro or acetyl;

W_3 is $-N(R_2)R_2$ wherein R_2 is propyl;

X is independently, a bond, methoxy ($-OCH_2-$), oxypropoxy ($-O(CH_2)_3O-$), hexenyloxy ($-O(CH_2)_4CH=CH-$), sulfonyloxy ($-SO_2O-$), methyl ($-CH_2-$), amidyl (-CONH-) or -NHCONH-;

and Y is either Y_1 or Y_2 then

Y_1 is croman, 4-H-chromen-4-one or napthalene optionally substituted with up to seven R_1 groups wherein R_1 is independently H, OH, methyl, ethyl, propyl, nitro, methoxy, ethoxy, 2-hydroxyethoxy, chloro, fluoro or acetyl;

Y_2 is 9H-xanthone optionally substituted with up to seven R_1 groups wherein R_1 is independently H, OH, methyl, ethyl, propyl, nitro, methoxy, ethoxy, 2-hydroxyethoxy, chloro, fluoro or acetyl;

Y_3 is phenyl optionally substituted with up to 5 R_1 groups wherein R_1 is independently H, OH, methyl, ethyl, propyl, nitro, methoxy, ethoxy, 2-hydroxyethoxy, chloro, fluoro or acetyl; and

Z is independently $-R_6COOH$, $-R_6SO_3H$ or -N-trifluoromesylsulfonamidate wherein R_6 is independently a bond or propyl.

10. A method according to claim 6, wherein the non-peptidyl compound is selected from the following group of compounds:

(i.) 4,4'-Methylenebis[3-hydroxy-2-naphthalenecarboxylic acid];

(ii.) 7-[3-(4-acetyl-2-ethyl-5-hydroxyphenoxy)propoxy]-3,4-dihydro-8-propyl-2H-1-benzopyran-2-carboxylic acid;

(iii.) 2,4-dichloro-6-(*N*-(trifluoromethanesulfonyl))sulfamoylphenyl 3,5-dichloro-2-hydroxybenzenesulfonate;

(iv.) 7-[(4-acetyl-3-hydroxy-2-propylphenyl)methoxy]-4-oxo-8-propyl-4*H*-1-benzopyran-2-carboxylic acid;

(v.) 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl-2*H*-1-benzopyran-2-carboxylic acid;

(vi.) 3,4-dihydro-8-propyl-7-[[3-[2-ethyl-5-hydroxy-4-(1*H*-pyrazol-3-yl)phenoxy]propyl]oxy]-2*H*-1-benzopyran-2-carboxylic acid;

(vii.) 3,4-dihydro-8-propyl-7-[[3-[2-ethyl-5-hydroxy-4-ethoxyphenoxy]propyl]oxy]-2*H*-1-benzopyran-2-carboxylic acid;

(viii.) 3-[4-[7-carboxy-9-oxo-3-[3-[2-ethyl-4-(4-fluorophenyl)-5-hydroxyphenoxy]propoxy]-9*H*-xanthene]]propanoic acid;

(ix.) 8-propyl-7-(quinol-2'-ylmethoxy)-3,4-dihydro-2*H*-1-benzopyran-2-carboxylic acid;

(x.) 7-(naphth-2'-ylmethoxy)-8-propyl-3,4-dihydro-2*H*-1-benzopyran-2-carboxylic acid;

(xi.) *N*-(trifluoromethanesulfonyl)-3,5-dinitro-4-(*N'*,*N'*-dipropylamino)benzenesulfonamide;

(xii.) 8-propyl-7-[3-[4-(4-fluorophenyl)-2-ethyl-5-hydroxyphenoxy]propoxy]-3,4-dihydro-2H-1-benzopyran-2-carboxylic acid;

(xiii.) 3,4-dihydro-7-[[6-(4-methoxyphenyl)hexenyl]oxy]-8-propyl-2H-1-benzopyran-2-carboxylic acid; or

(xiv.) 8,8'-[Carbonylbis[imino-3,1-phenylenecarbonylimino(4-methyl-3,1-phenylene)carbonylimino]]bis-1,3,5-naphthalenetrisulfonic acid.

11. A pharmaceutical composition comprising at least a chemical compound capable of modulating the biological activity of insulin, and a second composition selected

from the group consisting of a pharmaceutically acceptable carrier, a diluent, and combinations thereof; wherein said compound has the following general formula.

$AXYXZ_n$ (formula 1)

where A is W or VXW;

V is V_1 or V_2;

V is substituted with up to two X groups;

V_1 is a phenyl or 6 membered heteroaromatic ring, optionally substituted with up to 5 R_1 groups;

V_2 is a 5 member ring system which may incorporate up to 4 hetero atoms which may be independently a nitrogen atom, a nitrogen atom optionally substituted with R_2, oxygen or sulfur, the ring system being optionally substituted with up to 4 R_1 groups;

W is W_1 or W_2 or W_3;

W is substituted with up to two X groups;

W_1 is V_1;

W_2 is a fused bicyclic ring system comprising rings of 5 or 6 atoms, which may incorporate up to 4 hetero atoms, which may be independently a nitrogen atom, a nitrogen atom optionally substituted with R_2, oxygen or sulfur, the system being optionally substituted with up to seven R_1 groups;

W_3 is $-N(R_2)R'_2$;

R_1 is independently H, OH, alkyl, alkenyl, alkynyl, alkoxy, alkanol, hydroxyalkoxy, haloalkyl, haloalkoxy, halogen, SH, thioalkyl, cyano (-CN), $N(R_2)R'_2$, phenyl, phenyl optionally substituted with up to five alkyl groups of 1 to 3 carbon atoms or up to five halogen atoms, benzyl, phenethyl, nitro, $-COR_3$, $-R_5COR_3$, $-R_5SOR_3$, $-R_5SO_2R_3$, $-SO_2N(R_2)R'_2$ or azido;

R_2 and R'_2 are independently H, alkyl of 1 to 6 carbon atoms, alkenyl of 3 to 6 carbon atoms, alkynyl of 3 to 6 carbons, hydroxyalkyl of 2 to 6 carbons, alkoxy of 2 to 6 carbons, haloalkyl, haloalkenyl, haloalkoxy, benzyl, benzyl optionally substituted with up to four R_1 groups, phenylethyl, phenylethyl optionally substituted with up to four R_1 groups, arylalkyl, and where R_2 and R'_2 can also be joined to form cyclic structures;

R_3 is independently H, OH, alkyl, alkenyl, alkynyl, alkoxy, alkanol, hydroxyalkoxy, $-R_4N(R_2)R'_2$, mesyl, triflouromesyl, $-NHSO_2CH_3$ or $-NHSO_2CF_3$;

R_4 is independently a bond, alkyl, alkenyl or alkynyl;

X is independently, a bond, $-R_4N(R_2)R_4-$, $-R_4N=NR_4-$, $-R_4N(R_2)-N(R_2)R_4-$, $-R_4OR_4-$, $-R_4SR_4-$, $-R_5-$, $-R_5O-$, $-R_5S-$, $-R_5N(R_2)-$, -SO-, sulfonyl ($-SO_2-$), -CO-, -CONH-, -NHCONH-, -NHCO-, -CONHCO-, $-CON(R_2)-$, $-R_5COR_5-$, $-R_5COR_5N(R_2)R_5-$, $-N(R_2)CO-$ or $-R_4N(R_2)R_4COR_4-$;

R_5 is independently alkyl, alkenyl, alkynyl, alkoxy, alkanol, hydroxyalkoxy;

Y is either Y_1, Y_2 or Y_3;

Y is substituted with at least two, but optionally up to four X linking groups;

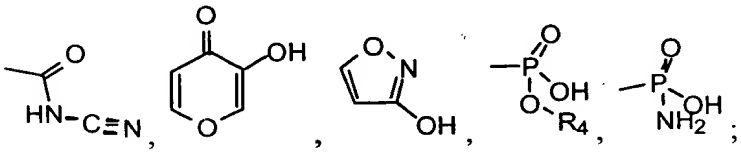
Y_1 is a fused bicyclic ring system comprising rings of 5 or 6 atoms which may incorporate up to 4 hetero atoms, which may be independently a nitrogen atom, a nitrogen atom optionally substituted with R_2, oxygen or sulfur, the ring system optionally independently incorporating a sulfoxide (SO), sulfone (SO_2) or carbonyl (CO) group and optionally up to seven R_1 groups;

Y_2 is a 6:6:6 or a 6:5:6 fused tricyclic system which may incorporate up to 4 hetero atoms which may be independently a nitrogen atom, a nitrogen atom optionally substituted with R_2, oxygen or sulfur, the ring system optionally independently incorporating a sulfoxide (SO), sulfone (SO_2) or carbonyl (CO) group, and the ring system being substituted with at least two, but optionally up to four X linking groups and optionally up to seven R_1 groups [and thus examples include, but are not limited to 9H-xanthone, 9H-xanthene, phenoxathaiin, phenoxathiin-10-oxide, phenoxathiin-10-dioxide, acridine, phenazine, phenothiazine, phenoxazine, phenothiazine-5-oxide, phenothiazine-5-dioxide, thiathrene-5-dioxide, thiathrene-5-oxide, carbazole, dibenzo[b,d]furan, dibenzo[b,d]thiophene];

Y_3 is V_1;

Z is independently $-R_6COOH$, $-R_6SO_3H$, $-R_6NO_2$, $-R_6SO_2H$, $-R_6SO_2NHR_2$; $-R_7SO_2NHCOR_4$ -N-trifluoromesylsulfonamidate, -OH, -2-yl-hydroxyethanoic acid (-CH(OH)COOH), -3-yl-2-hydroxypropanoic acid ($-CH_2CH(OH)COOH$) -2-yl-2-hydroxypropanoic acid ($-CH(CH_3)(OH)COOH$), -3-yl-2,3-dihydroxypropanoic acid (-CH(OH)CH(OH)COOH), -2-yl-2,3-dihydroxypropanoic acid (-

$C(CH_2(OH))(OH)COOH$), -3-yl-2-hydroxypropan-3-one-1-oic acid (-$COCH(OH)COOH$, 2-yl-2-hydroxypropandioic acid (-$C(COOH)(OH)COOH$), -2-yl-propandioic acid (-$C(COOH)(H)COOH$), -4-yl-2-hydroxybutan-4-one-1-oic acid (-$COCH_2CH(OH)COOH$, 2-yl-2-hydroxybutan-1,4-dioic acid (-$C(OH)(COOH)CH_2COOH$), 3-yl-2-hydroxybutan-1,4-dioic acid (-$CH(CH(OH)COOH)COOH$), 5-yl-tetrazole,



R_6 is independently a bond, alkyl, alkenyl, alkynyl, alkoxy, $-CO(CH_2)_n-$, where n is an integer between 0 and 4, alkanoic, alkenoic or alkynoic;

with the exception that where W_1 is an optionally substituted phenyl then Y_1 cannot be an optionally substituted phenyl.

12. A pharmaceutical composition according to claim 11, wherein the non-peptidyl compound is a dimer or heterodimer of compounds where such compounds are joined through a X linking group by way of their V or W groups.

13. A pharmaceutical composition according to claim 11, wherein when V is V_1 or V_2, then:

V_1 is selected from the group consisting of, benzene, pyridine, pyridazine, pyrimidine, pyrazine or triazine and is optionally substituted with up to 5 R_1 groups; and

V_2 is selected from the group consisting of, cyclopenta-1,3-diene, pyrrole, furan, thiophene, oxazole, isoxazole, pyrazole, imidazole, thiazole, isothiazole or triazole and is optionally substituted with up to 4 R_1 groups;

and W is W_2 then

W_2 is selected from the group consisting of naphthalene, quinoline, isoquinoline, phthalazine, naphthyridine, quinoxaline, quinazoline, cinnoline, pteridine, indole, benzothiophene, benzofuran, benzimidazole, indazole, benzoxazole, benzisooxazole, benzthiazole, benzisothiazole, purine, indoline or isoindoline and is optionally substituted with up to seven R_1 groups;

and Y is either Y_1 or Y_2 then

Y_1 is selected from the group consisting of croman, isochroman, benzofuran, cromene, 1,2,3,4-tetrahydronaphthalene, 1,4-dihydronaphthalene, indan, indene, benzopiperidine, indoline, isoindoline, quinoline, isoquinoline, phthalazine, naphthyridine, quinoxaline, quinazoline, cinnoline or pteridine, coumarin or 2,3-dihydrocoumarin and is optionally substituted with up to seven R_1 groups; and

Y_2 is selected from the group consisting of 9H-xanthone, 9H-xanthene, phenoxathiin, phenoxathiin-10-oxide, phenoxathiin-10-dioxide, acridine, phenazine, phenothiazine, phenoxazine, phenothiazine-5-oxide, phenothiazine-5-dioxide, thiathrene-5-dioxide, thiathrene-5-oxide, carbazole, dibenzo[b,d]furan or dibenzo[b,d]thiophene and is optionally substituted with up to seven R_1 groups.

14. A pharmaceutical composition according to claim 11, wherein in the non-peptidyl compound of formula 1 when A is W or VXW then:

V is phenyl or pyrazole, optionally substituted with up to 5 R_1 groups;

and W is W_1, W_2 or W_3 then,

W_1 is phenyl optionally substituted with up to 5 R_1 groups;

W_2 is naphthalene or quinoline optionally substituted with up to seven R_1 groups wherein R_1 is independently H, OH, methyl, ethyl, propyl, nitro, methoxy, ethoxy, 2-hydroxyethoxy, chloro, fluoro or acetyl;

W_3 is $-N(R_2)R_2$ wherein R_2 is propyl;

X is independently, a bond, methoxy ($-OCH_2-$), oxypropoxy ($-O(CH_2)_3O-$), hexenyloxy ($-O(CH_2)_4CH=CH-$), sulfonyloxy ($-SO_2O-$), methyl ($-CH_2-$), amidyl (-CONH-) or -NHCONH-;

and Y is either Y_1 or Y_2 then

Y_1 is croman, 4-H-chromen-4-one or napthalene optionally substituted with up to seven R_1 groups wherein R_1 is independently H, OH, methyl, ethyl, propyl, nitro, methoxy, ethoxy, 2-hydroxyethoxy, chloro, fluoro or acetyl;

Y_2 is 9H-xanthone optionally substituted with up to seven R_1 groups wherein R_1 is independently H, OH, methyl, ethyl, propyl, nitro, methoxy, ethoxy, 2-hydroxyethoxy, chloro, fluoro or acetyl;

Y_3 is phenyl optionally substituted with up to 5 R_1 groups wherein R_1 is independently H, OH, methyl, ethyl, propyl, nitro, methoxy, ethoxy, 2-hydroxyethoxy, chloro, fluoro or acetyl; and

Z is independently $-R_6COOH$, $-R_6SO_3H$ or -N-trifluoromesylsulfonamidate wherein R_6 is independently a bond or propyl.

15. A pharmaceutical composition according to claim 11, wherein the non-peptidyl compound is selected from the following group of compounds:

(xv.) 4,4'-Methylenebis[3-hydroxy-2-naphthalenecarboxylic acid];

(xvi.)7-[3-(4-acetyl-2-ethyl-5-hydroxyphenoxy)propoxy]-3,4-dihydro-8-propyl-2H-1-benzopyran-2-carboxylic acid;

(xvii.) 2,4-dichloro-6-(*N*-(trifluoromethanesulfonyl))sulfamoylphenyl 3,5-dichloro-2-hydroxybenzenesulfonate;

(xviii.) 7-[(4-acetyl-3-hydroxy-2-propylphenyl)methoxy]-4-oxo-8-propyl-4*H*-1-benzopyran-2-carboxylic acid;

(xix.) 7-[3-(4-acetyl-3-methoxy-2-propylphenoxy)propoxy]-3,4-dihydro-8-propyl-2*H*-1-benzopyran-2-carboxylic acid;

(xx.) 3,4-dihydro-8-propyl-7-[[3-[2-ethyl-5-hydroxy-4-(1*H*-pyrazol-3-yl)phenoxy]propyl]oxy]-2*H*-1-benzopyran-2-carboxylic acid;

(xxi.) 3,4-dihydro-8-propyl-7-[[3-[2-ethyl-5-hydroxy-4-ethoxyphenoxy]propyl]oxy]-2*H*-1-benzopyran-2-carboxylic acid;

(xxii.) 3-[4-[7-carboxy-9-oxo-3-[3-[2-ethyl-4-(4-fluorophenyl)-5-hydroxyphenoxy]propoxy]-9*H*-xanthene]]propanoic acid;

(xxiii.) 8-propyl-7-(quinol-2'-ylmethoxy)-3,4-dihydro-2*H*-1-benzopyran-2-carboxylic acid;

(xxiv.) 7-(naphth-2'-ylmethoxy)-8-propyl-3,4-dihydro-2*H*-1-benzopyran-2-carboxylic acid;

(xxv.) *N*-(trifluoromethanesulfonyl)-3,5-dinitro-4-(*N'*,*N'*-dipropylamino)benzenesulfonamide;

(xxvi.) 8-propyl-7-[3-[4-(4-fluorophenyl)-2-ethyl-5-hydroxyphenoxy]propoxy]-3,4-dihydro-2H-1-benzopyran-2-carboxylic acid;

(xxvii.)3,4-dihydro-7-[[6-(4-methoxyphenyl)hexenyl]oxy]-8-propyl-2H-1-benzopyran-2-carboxylic acid; or

(xxviii.)8,8'-[Carbonylbis[imino-3,1-phenylenecarbonylimino(4-methyl-3,1-phenylene)carbonylimino]]bis-1,3,5-naphthalenetrisulfonic acid.

16. A method for identifying a non-peptidyl compound possessing ionic and hydrophobic chemical moieties spatially located so as to mimic particular ionic and hydrophobic amino acid residues of insulin which are associated with the binding of insulin to its receptor, said method comprising the steps of: (1) comparing the three dimensional structure of the non-peptidyl compound with a three dimensional pharmacophore of an active site of insulin; and (2) selecting a non-peptidyl compound with ionic and hydrophobic chemical moieties spatially located so as to mimic said site.

17. A method for determining whether a non-peptidyl compound identified according to the method of claim 16 is an agonist or an antagonist, said method comprising the step of: exposing the compound to an insulin or insulin like receptor and measuring the change in biological activity following exposure of the compound to the receptor.

18. (Cancelled)

19. (Cancelled)

20. A method according to claim 6 wherein V_1 is selected from the group: benzene, pyridine, pyridazine, pyrimidine, pyrazine, triazine.

21. A method according to claim 6 wherein V_2 is selected from the group: cyclopenta-1,3-diene, pyrrole, furan, thiophene, oxazole, isoxazole, pyrazole, imidazole, thiazole, isothiazole or triazole, optionally substituted with up to 4 R_1 groups.

22. A method according to claim 6 wherein W_2 is selected, from the group: naphthalene, quinoline, isoquinoline, phthalazine, naphthyridine, quinoxaline, quinazoline, cinnoline, pteridine, indole, benzothiophene, benzofuran, benzimidazole, indazole, benzoxazole, benzisooxazole, benzthiazole, benzisothiazole, purine, indoline, isoindoline.

23. A method according to claim 6 wherein R_2 and R'_2 are joined to form cyclic structures selected from the group: pyrrolidine, piperidine, hexahydro-1H-azepine, morpholine or piperazine.

24. A method according to claim 6 wherein Y_1 is selected from the group: croman, isochroman, benzofuran, cromene, 1,2,3,4-tetrahydronaphthalene, 1,4-dihydronaphthalene, indan, indene, benzopiperidine, indoline, isoindoline, quinoline, isoquinoline, phthalazine, naphthyridine, quinoxaline, quinazoline, cinnoline or pteridine, coumarin or 2,3-dihydrocoumarin.

25. A method according to claim 6 wherein Y_2 is selected from the group: 9H-xanthone, 9H-xanthene, phenoxathiin, phenoxathiin-10-oxide, phenoxathiin-10-dioxide, acridine, phenazine, phenothiazine, phenoxazine, phenothiazine-5-oxide, phenothiazine-5-dioxide, thiathrene-5-dioxide, thiathrene-5-oxide, carbazole, dibenzo[b,d]furan, dibenzo[b,d]thiophene.

26. A pharmaceutical composition according to claim 11 wherein V_1 is selected from the group: benzene, pyridine, pyridazine, pyrimidine, pyrazine, triazine.

27. A pharmaceutical composition according to claim 11 wherein V_2 is selected from the group: cyclopenta-1,3-diene, pyrrole, furan, thiophene, oxazole, isoxazole, pyrazole, imidazole, thiazole, isothiazole or triazole, optionally substituted with up to 4 R_1 groups.

28. A pharmaceutical composition according to claim 11 wherein W_2 is selected, from the group: naphthalene, quinoline, isoquinoline, phthalazine, naphthyridine, quinoxaline, quinazoline, cinnoline, pteridine, indole, benzothiophene, benzofuran, benzimidazole, indazole, benzoxazole, benzisooxazole, benzthiazole, benzisothiazole, purine, indoline, isoindoline.

29. A pharmaceutical composition according to claim 11 wherein R_2 and R'_2 are joined to form cyclic structures selected from the group: pyrrolidine, piperidine, hexahydro-1H-azepine, morpholine or piperazine.

30. A pharmaceutical composition according to claim 11 wherein Y_1 is selected from the group: croman, isochroman, benzofuran, cromene, 1,2,3,4-tetrahydronaphthalene, 1,4-

dihydronaphthalene, indan, indene, benzopiperidine, indoline, isoindoline, quinoline, isoquinoline, phthalazine, naphthyridine, quinoxaline, quinazoline, cinnoline or pteridine,. coumarin or 2,3-dihydrocoumarin.

31. A pharmaceutical composition according to claim 11 wherein Y_2 is selected from the group: 9H-xanthone, 9H-xanthene, phenoxathiin, phenoxathiin-10-oxide, phenoxathiin-10-dioxide, acridine, phenazine, phenothiazine, phenoxazine, phenothiazine-5-oxide, phenothiazine-5-dioxide, thiathrene-5-dioxide, thiathrene-5-oxide, carbazole, dibenzo[b,d]furan, dibenzo[b,d]thiophene.